IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	: Simons *et al.*
Serial No.	: 09/145,916
Filed	: September 2, 1998
For	: "STIMULATION OF ANGIOGENESIS VIA ENHANCED ENDOTHELIAL EXPRESSION OF SYNDECAN-4 CORE PROTEINS"
Examiner	: David Guzo
Group Art Unit	: 1636
Attorney's Docket No	: BIS-039

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to Commission for Patents, P.O. Box 1450, Mail Stop: RCE, Alexandria, Virginia 22313-1450 on: _____.

Attorney for applicants: _____

Signature: _____

Date: _____

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MARKED UP VERSION OF AMENDED SPECIFICATION SUBMITTED
PURSUANT TO 37 C.F.R.1.121(b)(1) (iii)

Commissioner for Patents
P.O. Box 1450
Mail Stop: RCE
Alexandria, Virginia 22313-1450

Sir:

In support of the Request for Continuing Examination and the substantive Response to the most recently received (final) Official Action as well as in fulfillment of and in accordance with the requirements of 37 C.R.F. 121(b)(1)(iii), applicants hereby submit a marked up version of the instant amendments to the Specification via marked-up replacement paragraphs, these Specification amendments being directed to paragraphs at:

Page 29, lines 19-20.

Respectfully submitted,

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C. The Cytoplasmic Domain Coding For The Syndecan-4 Peptide

The third requisite cytoplasmic domain must code for the amino acid residue structure representative of the syndecan-4 core protein. As shown experimentally by the data presented hereinafter, only the syndecan-4 cytoplasmic region and peptide structure allows for functional stimulation of angiogenesis in-situ. For this reason, it is essential and required in each embodiment of the present invention that the third DNA sequence coding for the cytoplasmic domain in the expressed proteoglycan entity in a transfected endothelial cell be representative of and analytically identifiable as the syndecan-4 amino acid residue structure. A representative recitation of the DNA constituting the cytoplasmic domain of the syndecan-4 molecule is presented by Fig. 13 herein.

It will be noted and recognized that very little variability and substitution within the specific DNA base sequencing of the cytoplasmic domain of the syndecan-4 molecule is permitted. While some changes are expected, be they point mutations, block substitutions and the like, the expected or envisioned degree of variability which might be present or permitted for the cytoplasmic domain DNA is believed to be quite limited.

As representative examples: The last four amino acids (EFYA) [SEQ ID NO:25] cannot be changed or modified. Similarly, regarding the Serine residue at position 181: a mutation to an Alanine residue potentiates activation; while a mutation to Glutamate inhibits cell growth in a dominant fashion (dominant-negative mutation). Finally, the LGKKPIYKK sequences [SEQ ID NO:24] probably cannot be altered at all.